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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,917	04/11/2006	Yipu Feng	13695/1	5543

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,917	FENG ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-8* is/are pending in the application.

4a) Of the above claim(s) *4-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election, with traverse, with the Group III (Group C) is acknowledged. Claims 6-8 read on the elected invention. There is no claim 9 presented in the pending claims.

Applicants traverse the restriction requirement on the grounds that claims 4-5 have unity of invention with claims 6-8 since these claims share the special technical feature of preventing or treating cerebral infarct in human beings with L-butylphthalide of formula (I). This argument is not persuasive, as claimed invention would be distinctive, each from the other because the technical feature such as L-butyphthalide of formula (I) linking Groups I-III (A-C) does not constitute a special technical feature, as it does not define a contribution over the prior art.

Thus, the requirement is still deemed proper, and made Final. Claims 4-5 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cerebral infarct with a compound of formula (I), does not reasonably provide enablement for "preventing cerebral infarct". The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for preventing or treating cerebral infarct comprising administering a compound of formula (I), namely l-n-butylphthalide, to a subject in need thereof.

The American Heritage Dictionary (Second College Edition, 1982) defines the "prevent" as "anticipate or counter in advance, to keep from happening". The interpretation of the instant claims allows for the complete cure and eradication or total elimination of cerebral infarct by the administration of said compound.

It is known today that "an effective treatment to improve brain ischemic injury has not yet been established…Therefore, novel therapeutics are needed to treat these

patients" (see page 424, column 1, paragraph 1 of Shimamura et al., Cir 109:424-431, 2004) and that "At present, no effective therapy or management strategy is available for reducing acute cerebral infarction mortality and/or disability" (see Page 662, column 1, paragraph 1 of Guo et al., Chin Med J 119(6):662-668, 2006). Thus, it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" or completely cure or eradication effect.

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art are high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the preventive utility of the instant compounds.

The specification provides the effects of l-n-butylphthalide in reducing cerebral infarct volume of animal study model (in vivo). However, there is no demonstrated correlation that the tests and results apply to the claimed preventive utility embraced by the instant claims.

Since the efficacy of the claimed compound(s) in preventing the cerebral infarct mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Feng et al. (CN 1257706).

The American Heritage Dictionary (Second College Edition, 1982) defines "prevent" as "anticipate or counter in advance, to keep from happening". To the extent that the claims 6-8 encompass methods of preventing cerebral infarct, the instant claims 6-8 are construed to read on any method of treatment employing the administering of the instant claimed compounds as the term "preventing" or "prophylactic" are construed to mean the absolute absence of cerebral infarct. In other words, the analysis of the instant claims 6-8 allows for the inclusion of any patient population ("a subject in need of such prevention"), as long as the same compound is administered to body of the patient in overlapping dosage amounts.

Feng teaches use of butylphthalide, preferably l-3-butylphthalide, as effective agent for curing thrombosis and thrombocyte coagulation, (abstract), wherein said compound is administered in dosage amounts in range from 5mg-200mg/kg to a subject (Figures).

Although Feng is silent about the activity of said l-3-butylphthalide in preventing cerebral infarct, such property or characteristic deems to be inherent to the referenced - method of administering same compound to a subject. Since the administration of the same compound or composition in overlapping dosage amounts to a subject inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by the applicant anticipates the claimed invention even absent explicit recitations of the underlying mechanism.

Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

4. Claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiong et al. (Yaoxue Xuebao, 2000, 35(6), pp. 408-412).

Xiong teaches use of butylphthalide including l-3-butylphthalide as effective agent for improving mitochondrial injury during cerebral ischemia (abstract), wherein said compound is administered in dosage amounts in range from 5mg-10mg/kg to a subject (Figures).

Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of

compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

5. Claims 6-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Chang et al. (Acta Pharmacologica Sinica, August 2003, 24(8), pp. 796-804).

Chang teaches use of 3-n-butylphthalide, preferably l-3-butylphthalide as effective agent for improving ischemia-induced apoptosis, particularly transient focal cerebral ischemia-apoptosis (abstract; para. 3 of page 803), wherein said compound is administered in dosage amounts in range from 5mg-20mg/kg to a subject (Figures).

Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xiong et al. (Yaoxue Xuebao, 2000, 35(6), pp. 408-412) or Chang et al. (Acta Pharmacologica Sinica, August 2003, 24(8), pp. 796-804).

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Alternatively assuming arguendo that the treatment population(s) discussed in above 35 USC 102(b) and 102(a) rejection differ(s) from the instant invention, such determination is considered obvious under the meaning of 103(a) as followings.

As similar to the instant animal model study, a person having ordinary skill in the art has basis for perceiving those studies provided in Xiong or Chang as constituting recognized procedure with clear relevance to utility in humans.

Applicant has presented no evidence to establish the unexpected or unobvious nature of the claimed invention, and as such, claims 608 are properly rejected under 35 U.S.C. 103.

Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 6-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending US application No. 11/629964.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed prophylactic utility of L-n-butylphthalide in preventing cerebral infarct would necessarily occur if the compounds of the '964 application is administered to the same subject.

As discussed above, to the extent that the claims 6-8 encompass methods of preventing cerebral infarct, the instant claims 6-8 are construed to read on any method of treatment employing the administering of the instant claimed compounds as the term "preventing" or "prophylactic" are construed to mean the absolute absence of cerebral infarct. In other words, the analysis of the instant claims 6-8 allows for the inclusion of any patient population ("a subject in need of such prevention"), as long as the same compound is administered to body of the patient in overlapping dosage amounts. Thus, the copending application makes obvious the instant invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614